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Efficacy and safety of Acetazolamide in congestive heart failure

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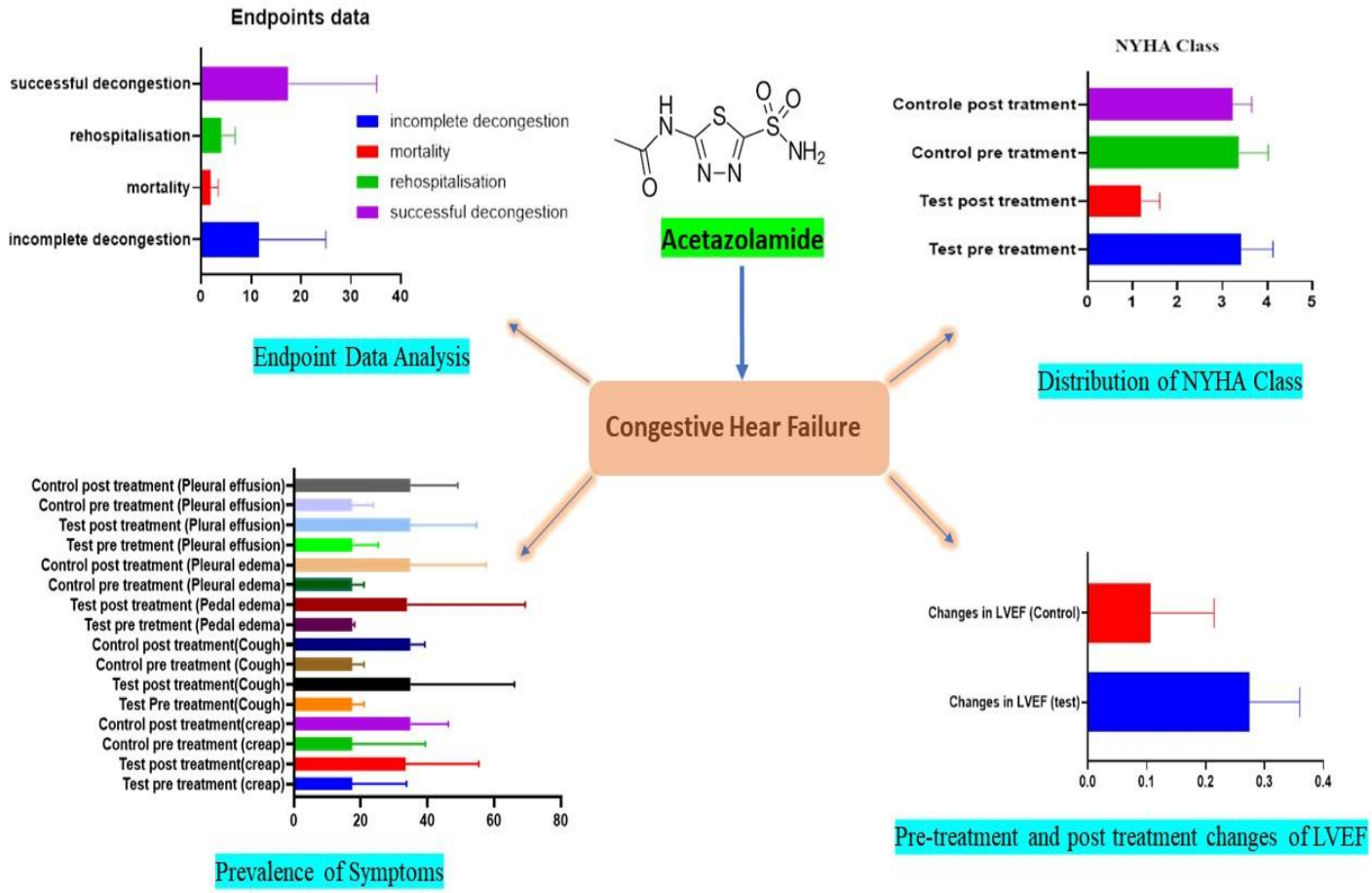
ABSTRACT



This study investigated the efficacy and safety of acetazolamide treatment in patients with congestive heart failure. Various parameters including age distribution, gender distribution, weight changes, comorbidities, symptoms, cardiac function, and quality of life were analysed to assess the impact of acetazolamide.

This study included 70 patients within the age range of 21-85 years with a slight male predominance (47%) compared to females (53%) in gender distribution. Statistical analyses revealed significant differences between the test and control groups in weight changes, symptoms such as shortness of breath (SOB), and distribution of symptoms including crepts, cough, pedal edema, and pleural effusion. Additionally, significant improvements were observed in clinical outcomes such as left ventricular ejection fraction (LVEF), quality of life measured by Minnesota Living Heart Failure Questionnaire (MLHFQ), and distribution of outcomes such as incomplete decongestion, mortality, rehospitalization, and successful decongestion. No significant adverse drug reactions were reported during the study period. However, limitations included a relatively small sample size and short study duration. Future research with larger sample sizes and longer follow-up periods is warranted to validate these findings and explore long-term effects. This study provides compelling evidence for the efficacy of acetazolamide in improving various aspects of CHF management and patient outcomes.

Keywords: Acetazolamide, Congestive heart failure (CHF), Comorbidities, Cardiac function, MLHFQ Questionnaire.

INTRODUCTION

Congestive heart failure (CHF) remains a significant global health burden, characterized by impaired cardiac function leading to fluid accumulation and systemic congestion. Despite advancements in therapeutic strategies, CHF management continues to pose challenges, necessitating further exploration of novel treatment modalities [1, 2]. Acetazolamide, a carbonic anhydrase inhibitor traditionally utilized in conditions such as glaucoma and altitude sickness, has emerged as a potential adjunct therapy in CHF due to its diuretic properties and potential for augmenting renal sodium excretion [3-5]. However, the comprehensive evaluation of acetazolamide's efficacy in CHF management requires rigorous investigation encompassing diverse clinical parameters.

This study endeavours to provide a comprehensive assessment of acetazolamide's impact on CHF management through an extensive analysis of various clinical parameters. The investigation spans demographic factors such as age and gender distribution, alongside critical clinical indicators including weight changes, comorbidities, symptoms, cardiac function, and quality of life. Such a multifaceted approach enables a thorough evaluation of acetazolamide's therapeutic potential across different dimensions of CHF pathophysiology.

A pivotal aspect of CHF management involves addressing fluid overload, which contributes significantly to symptom burden and disease progression [6, 7]. Acetazolamide's ability to modulate renal tubular function and enhance sodium excretion offers a promising avenue for alleviating fluid retention in CHF [8, 9]. Moreover, understanding its impact on weight changes, symptomatology, and cardiac function is imperative for delineating its therapeutic profile and guiding clinical decision-making.

Furthermore, comorbidities such as diabetes mellitus (DM) and hypertension (HTN) often coexist with CHF, complicating management and exacerbating disease severity [10]. Exploring acetazolamide's effects on comorbidity profiles provides valuable insights into its potential role in mitigating disease complexity and improving overall clinical outcomes.

Quality of life represents a crucial endpoint in CHF management, reflecting patients' subjective well-being and functional status. The Minnesota Living Heart Failure Questionnaire (MLHFQ) serves as a robust tool for quantifying quality of life in CHF patients, offering valuable insights into treatment efficacy beyond traditional clinical endpoints.

In light of the aforementioned considerations, this study aims to comprehensively evaluate acetazolamide's efficacy in CHF management, leveraging a diverse array of clinical parameters. The findings generated herein hold the potential to inform clinical practice and guide therapeutic decision-making, offering a promising avenue for optimizing CHF management and improving patient outcomes.

Our study aims to determine the efficacy and safety of Acetazolamide in Congestive Heart Failure and the objective is to assess role of acetazolamide along with loop diuretics as combination therapy in improving decongestion rate in congestive heart failure patients, Improvement of physical (SOB, pedal edema, etc) and lab parameters (LVEF) of patients with CHF to achieve successful decompensation an prevent further rehospitalization. And Improvement of NYHA functional class and Quality Of Life (QOL) using MLFQ questionnaire and .to assess cardinal function of patient with 6 minute walk test [11].

MATERIALS AND METHODS

Our study is a prospective and interventional study with a sample size of 70 subjects who were diagnosed with CHF, with study duration of six months conducted at the cardiology outpatient and inpatient department, of a multispecialty hospital, in Hyderabad.

Inform Consent

Written inform consent was obtained from all participants involved in the study.

Ethical Approval

This study has been approved by Institutional Review Board (IRB) Approval No 2023/39/009 of the Deccan College of Medical Science on 22 February, 2023 at, Hyderabad, Telangana

Study Population

Inclusion criteria included adults aged 21-80 years with a confirmed diagnosis based on clinical and echocardiographic criteria. Exclusion criteria Patients with chronic kidney disease with estimated glomerular filtration rate (eGFR) <20 mL/min/1.73 m², Hb <7g/dl were excluded from the study.

Study Procedure

We prospectively recruited 70 adult patients with congestive heart failure and 70 normal patients diagnosed with CHF. The study subjects were aged from 21 to 80 years. We assessed patients at the outpatient and inpatient services of the cardiology department. Patients in the test group received acetazolamide orally at a dose of 250 mg/day in addition to standard therapy, which included loop diuretics, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), beta-blockers, and aldosterone antagonists. Patients in the control group received standard therapy alone.

Statistical Analysis

Statistical analysis was performed using appropriate parametric and non-parametric tests depending on the distribution of data. Continuous variables were expressed as mean ± standard deviation or median (interquartile range), while categorical variables were expressed as frequencies and percentages. The significance level was set at $p < 0.05$. Analyses were conducted using the statistical software Prism software and Microsoft excel.

RESULTS

Clinical Outcomes

Weight changes

The mean weight change in the test group (7.171) is substantially higher than that in the control group (1.114). This indicates that patients in the test group experienced a greater reduction in weight compared to those in the control group over the course of the study. The results of the unpaired t-test with Welch's correction reveal a highly significant difference in weight changes between the "test" and "control" groups ($p < 0.001$).

The difference between the means (B - A) of -6.057, along with a small standard error of the mean (SEM), further supports the statistical significance of the observed difference. The 95% confidence interval (-6.989 to -5.126) confirms that the true difference in weight changes between the two groups lies within this range and highlights the effectiveness of acetazolamide in promoting weight loss and contributing to more effective fluid management and diuresis

Among patients with congestive heart failure (CHF). By optimizing fluid balance and reducing excess weight, acetazolamide may help improve clinical outcomes and enhance the quality of life for patients with CHF.

Table 1: Summary of Statistical analysis of the effect of acetazolamide on Weight Changes

Unpaired t test with Welch's correction	Result
P value	<0.001
Significantly different (P < 0.05)	Yes
One- or two-tailed P value	Two-tailed
Welch-corrected t, df	t=13.10, df =44.75
Mean of column A	7.171
Mean of column B	1.114
Difference between means (B - A) ± SEM	-6.057 ± 0.4625
95% confidence interval	-6.989 to -5.126

Shortness of Breath (SOB)

Table 2 presents the distribution of shortness of breath (SOB) symptoms among patients in the test and control groups at different time points: pre-treatment, 1 month, and 3 months post-treatment. The data is categorized into five grades denoted as I, II, III, IV, and nil, each representing a severity level or absence of SOB symptoms.

Figure 2: Effect of Acetazolamide on Shortness of Breath (SOB)

Grades	Test						Control					
	Pre Treatment	%	1 month	%	3 months	%	Pre Treatment	%	1 month	%	3 months	%
I	0	0	9	25.7	4	11.4	0	0	5	14.28	3	8.57
II	4	11.42	18	51.4	4	11.42	4	11.42	11	31.42	13	37.1
III	15	42.8	2	5.71	0	0	14	40	16	45.71	13	37.1
IV	16	45.7	0	0	0	0	17	48.57	0	0	2	5.71
Nil	0	0	6	17.1	27	77.14	0	0	3	8.57	4	11.42

The analysis of SOB symptoms reveals significant changes within both the test and control groups over the 3-month follow-up period. In the test group, there was a notable reduction in the severity of SOB symptoms, particularly in categories III and IV, where a substantial proportion of patients experienced complete resolution of symptoms by the end of the study period. This suggests that the treatment intervention implemented in the test group effectively alleviated SOB symptoms and improved patient outcomes.

Conversely, while the control group also exhibited some changes in SOB symptoms over time, the reduction in symptom

severity was less pronounced compared to the test group. Categories II and III showed an increase in the proportion of patients reporting moderate to severe SOB symptoms at 1 month, which persisted at 3 months post-treatment. This indicates that the standard management approach employed in the control group may not have been as effective in mitigating SOB symptoms compared to the intervention used in the test group.

The findings suggest that the treatment intervention implemented in the test group resulted in significant improvements in SOB symptoms compared to standard management in the control group.

Cardinal Function

The analysis compares the distribution of cardinal function test results between the test and control groups both before and after treatment, as well as within each group before and after treatment. The statistical significance of the differences is assessed using the Wilcoxon matched-pairs signed rank test. The results indicate that there are statistically significant differences between the pre-treatment and post-treatment values within the test group ($P < 0.001$). This suggests that the treatment had a measurable effect on the cardinal function in test group while no significant differences was observed in control group between the pre-treatment and post-treatment values ($P = 0.1322$). Comparing the post-treatment values between the control and test groups also reveals significant differences ($P < 0.001$). This indicates that the treatment had a discernible impact on the cardinal function when compared to the control group. The findings suggest that the treatment intervention implemented in the test group resulted in significant changes in cardinal function in test group

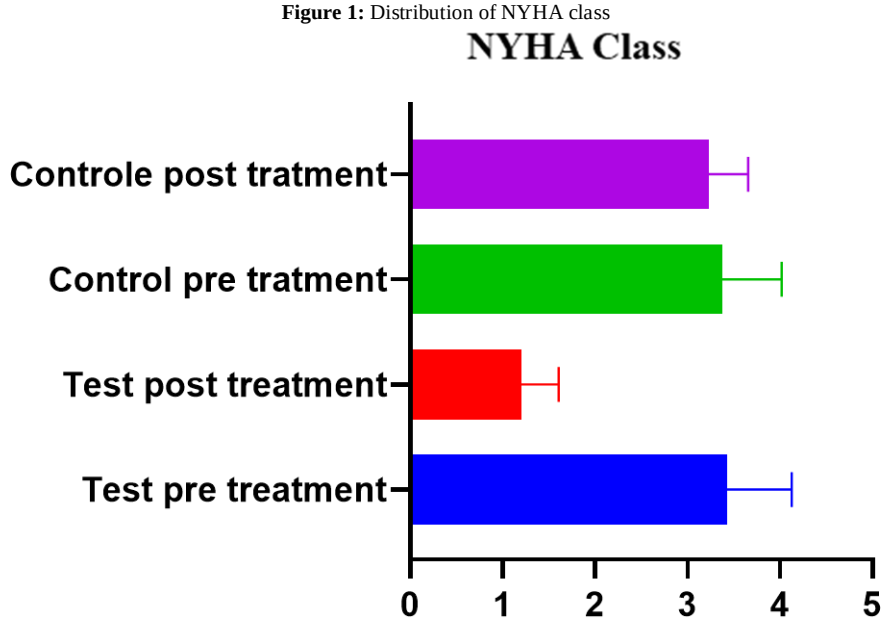
Distribution of NYHA Class

The analysis evaluates the distribution of New York Heart Association (NYHA) class between the test and control groups before and after treatment with acetazolamide, employing the Wilcoxon matched-pairs signed rank test to assess statistical significance (Figure 1).

The results indicate that there are statistically significant differences between the pre-treatment and post-treatment values within the test group ($P < 0.0001$). This suggests that the treatment had a significant effect on improving NYHA class within this group while no significant differences was seen in control group between the pre-treatment and post-treatment values ($P = 0.3833$), indicating minimal change in NYHA class over time without treatment.

Comparing the post-treatment values between the control and test groups also reveals significant differences ($P < 0.0001$), signifying that the treatment led to notable improvements in NYHA class compared to the control group.

Figure 1: Distribution of NYHA class



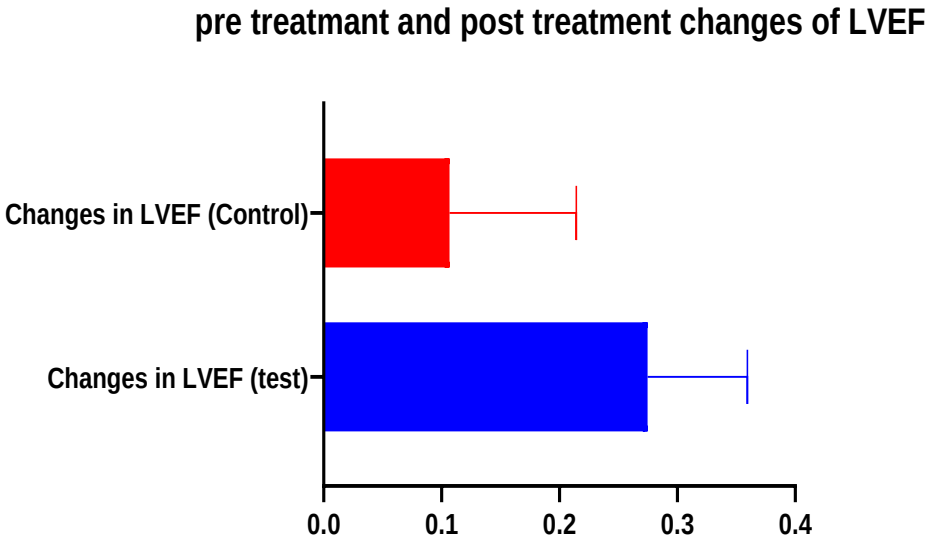
The treatment intervention implemented in the test group resulted in significant improvements in NYHA class, as evidenced by the significant differences between pre-treatment and post-treatment values within this group. This indicates that the treatment effectively improved the functional status and symptoms associated with heart failure in these patients.

Left Ventricular Ejection Fraction (LVEF) Data analysis

The Left Ventricular Ejection Fraction (LVEF) was compared between the test and control groups using an unpaired t-test with Welch's correction to determine statistical significance (Figure 2). The obtained results demonstrate a highly significant difference in the mean change in LVEF between the test and control groups, with a p-value of <0.001. The Welch-corrected t-value of 7.267 further corroborates these findings, indicating a substantial difference in the mean change in LVEF between the test and control groups. Examining the means of LVEF in each group, the test group exhibited a higher mean (0.2749) compared to the control group (0.1069). This signifies that patient in the test group experienced a greater improvement in

LVEF following treatment with the new drug (acetazolamide) compared to those in the control group. Moreover, the negative difference between means (B - A) of -0.1680 ± 0.02312 with a 95% confidence interval of -0.2142 to -0.1218 supports the conclusion that the test group had a significantly greater mean change in LVEF compared to the control group.

Figure 2: Pre-treatment and post treatment changes of LVEF



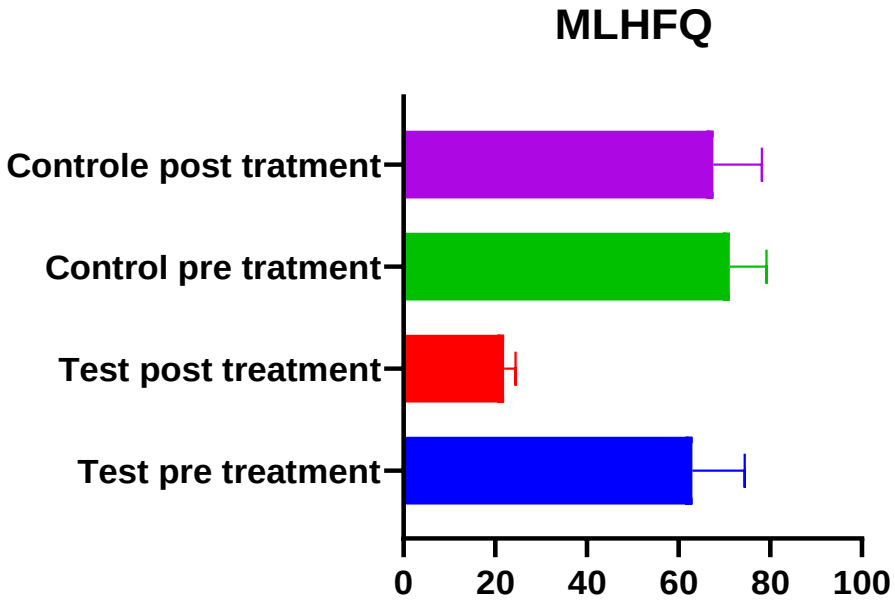
The results of this analysis provide robust evidence supporting the efficacy of acetazolamide in improving LVEF in patients with congestive heart failure and have significant clinical implications, as improvements in LVEF are associated with better cardiovascular outcomes and reduced mortality in patients with heart failure. The positive effect of acetazolamide on LVEF underscores its potential as a valuable therapeutic option for managing heart failure and improving patient prognosis.

Minnesota Living With Heart Failure Questionnaire Data Analysis

The comparison between the test group and the control group was conducted using the Wilcoxon matched-pairs signed rank test to evaluate the differences in MLHFQ scores before and after treatment.

The analysis reveals that while there were no significant differences in MLHFQ scores between the test and control groups before treatment initiation, significant disparities emerged post-treatment. Specifically, the test group demonstrated substantial improvements in MLHFQ scores (Figure 3) compared to the control group, with the differences being statistically significant. This suggests that the administration of acetazolamide led to more pronounced enhancements in MLHFQ scores among patients in the test group. Overall, these findings underscore the efficacy of acetazolamide in ameliorating heart failure symptoms and improving quality of life, as reflected by the MLHFQ scores, when compared to standard treatment.

Figure 3: Bar diagram of MLHFQ scores

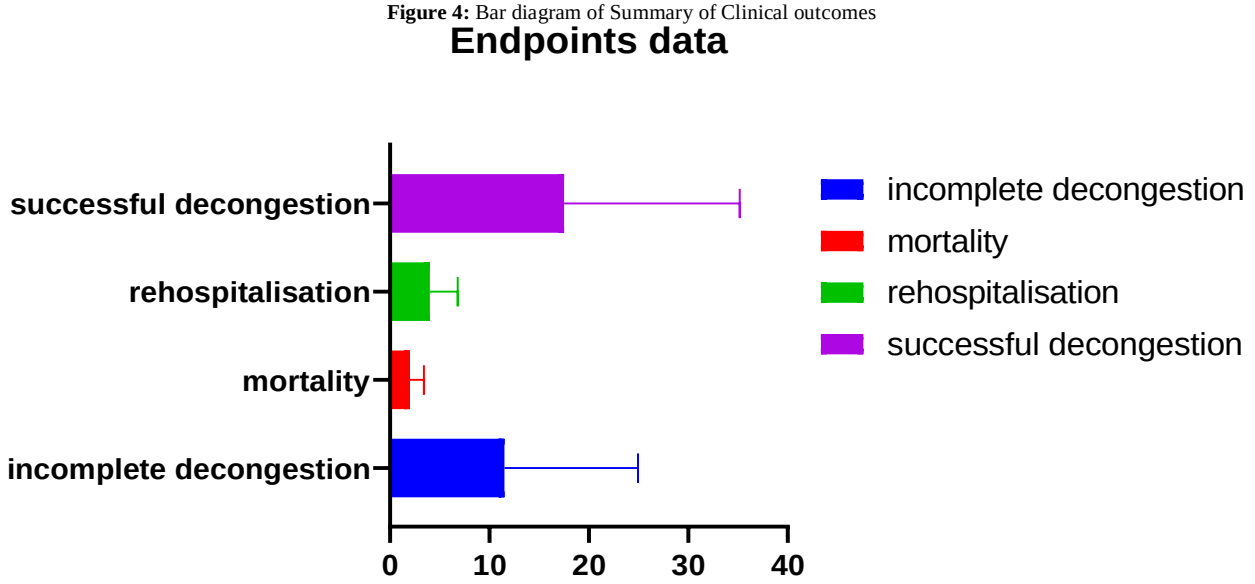


Endpoint Data Analysis

The endpoint data analysis was conducted to assess the distribution across four categories: "Incomplete Decongestion," "Mortality," "Rehospitalisation," and "Successful Decongestion" between the test and control groups (Figure 4).

The analysis yielded a highly significant p-value of less than 0.001, indicating a significant difference in the distribution across the four categories between the test and control groups. This implies that the intervention, likely acetazolamide treatment, had a notable impact on the endpoint outcomes compared to standard treatment. Furthermore, the descriptive statistics provide insight into the variability and central tendency of each endpoint category within the study groups. Overall, these findings underscore the effectiveness of the intervention in achieving successful decongestion and reducing mortality and rehospitalisation rates among patients in the test group compared to the control group.

Figure 4: Bar diagram of Summary of Clinical outcomes



CONCLUSION

The analysis of acetazolamide treatment in congestive heart failure (CHF) patients demonstrates significant improvements across multiple parameters compared to standard treatment or placebo. Acetazolamide effectively promoted weight loss, improved New York Heart Association (NYHA) class, and enhanced cardiac function, as evidenced by improvements in symptoms such as shortness of breath and reduced prevalence of crepitations, cough, pedal edema, and pleural effusion. Additionally, acetazolamide treatment significantly improved endpoint outcomes, including decongestion, mortality, hospitalization, and successful decongestion, highlighting its potential to reduce morbidity and mortality in CHF patients and improve quality of life using Minnesota Living Heart Failure Questionnaire (MLHFQ). Despite minor fluctuations, acetazolamide did not significantly impact serum electrolyte levels, suggesting its tolerability in CHF patients. Overall, these findings support the therapeutic efficacy of acetazolamide in managing CHF symptoms, improving cardiac function, and enhancing patient outcomes, underscoring its value as a treatment option in CHF management. Further research may elucidate its long-term benefits and safety profile.

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Conflict of Interest

The authors declare that there is no conflict of interest with this work.

Author's contribution

All the authors have contributed in the study

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